

C-A-S- 4/23/81

09/730,380

Page 1

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L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2001 ACS  
AN 2000:725436 CAPLUS  
DN 133:301171  
TI Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents  
IN Chen, Feng-jing; Patel, Manesh V.  
PA Lipocene, Inc., USA  
SO PCT Int. Appl., 99 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

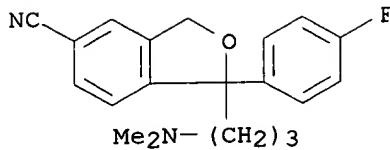
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000059475	A1	20001012	WO 2000-US7342	20000316
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			US 1999-287043 A 19990406

AB The present invention is directed to a **pharmaceutical compn.** including a hydrophobic therapeutic agent having at least one ionizable functional group, and a carrier. The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers, triglycerides, and neutralizing agents. The invention further relates to a method of prep. such compns. by providing a compn. of an ionizable hydrophobic therapeutic agent, an ionizing agent, and a surfactant, and neutralizing a portion of the ionizing agent with a neutralizing agent. The compns. of the invention are particularly suitable for use in oral dosage forms. A carrier contg. concd.

phosphoric acid 0.025, Tween-20 0.3, Arlacet 186 0.2, sodium taurocholate 0.15, propylene glycol 0.3 g was formulated. Itraconazole was included in the carrier at 30 mg/mL for testing the stability of the itraconazole soln. upon diln. in simulated gastric fluid.

IT 59729-33-8, Citalopram  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. contg. hydrophobic therapeutic agents and carriers contg. ionizing agents and surfactants and triglycerides)

RN 59729-33-8 CAPLUS  
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RE.CNT 3

RE

- (1) Blair; US 4306981 A 1981 CAPLUS
- (2) Hauer; US 5342625 A 1994 CAPLUS
- (3) Story; US 4944949 A 1990 CAPLUS

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 2000:210388 CAPLUS

DN 132:246337

TI Altering patterns of activity of drug metabolizing enzymes in patients to improve the effectiveness of drugs or activation of prodrugs

IN Slanetz, Alfred

PA Transgene S.A., Fr.

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000017366	A2	20000330	WO 1999-EP6973	19990921
	WO 2000017366	A3	20000713		
	W: AU, CA, JP			US 1998-157366 A	19980921
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,			AU 1999-63280	19990921
	PT, SE			US 1998-157366 A	19980921
				WO 1999-EP6973 W	19990921

AB Provided are pharmaceutical compns. for the pre-treatment of a patient in need of a drug or a pro-drug wherein said drug or pro-drug is over- or under-metabolized in said patient, and uses of such **pharmaceutical compn.** The method involves either raising or lowering the level of a drug metabolizing enzyme such as a cytochrome P 450 isoenzyme assocoated.

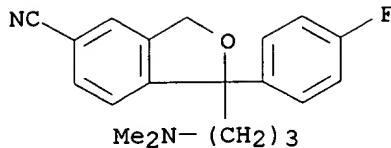
with the catabolism of a drug or the activation of a prodrug to ensure that the drug maintains a therapeutically useful level for a longer time than is typical for a given patient. The method can be extended to using a combination of enzymes that act at different stages in the treatment to maximize drug effectiveness.

IT 59729-33-8, Citalopram

RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(cytochrome P 450 metab. of; altering patterns of activity of drug metabolizing enzymes in patients to improve effectiveness of drugs or activation of prodrugs)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 2000:190921 CAPLUS

DN 132:241949

TI **Pharmaceutical compositions** containing NAD 299 and citalopram

IN Evenden, John; Thorberg, Seth-Olov

PA Astra Aktiebolag, Swed.

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015219	A1	20000323	WO 1999-SE1598	19990913
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			SE 1998-3157	A 19980916
	AU 9963781	A1	20000403	AU 1999-63781	19990913
				SE 1998-3157	A 19980916
				WO 1999-SE1598	W 19990913

AB A **pharmaceutical compn.** comprising a first component (a) which is (R)-3- N,N -dicyclobutylamino-8-fluoro-3,4-dihydro-2-H-1-benzopyran-5-carboxamide hydrogen-(2R,3R)-tartrate monohydrate (NAD 299) and a second component (b) which is citalopram, as the racemate or an enantiomer thereof in the form of its free base, or a pharmaceutically acceptable salt and/or solvate thereof, the prepn. thereof,

pharmaceutical

formulations contg. said compn., use of and a method of treatment of affective disorders such as mood disorders and anxiety disorders with said

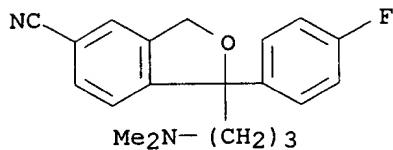
compn. as well as a kit contg. said compn. are disclosed. S.c. administration of 0.3 mg/kg NAD 299 60 min after injection of 5 mg/kg citalopram to rats strongly potentiated the 5-HT elevating action of citalopram vs. controls. A pharmaceutical tablet contained NAD 299 5, citalopram 20, microcryst. cellulose 100, corn starch 40, povidone 4, water 50, sodium starch glycolate 8, and magnesium stearate 1 mg.

IT 59729-33-8, Citalopram

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. contg. NAD 299 and citalopram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RE.CNT 1

RE

(1) Astra Aktiebolag; WO 9633710 A1 1996 CAPLUS

L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1999:282100 CAPLUS

DN 130:316651

TI Synergistic pharmaceutical compositions containing moxonidine

IN Perry, Kenneth Wayne

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

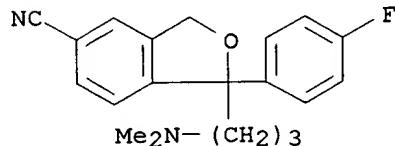
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9920279	A1	19990429	WO 1998-US21418	19981009
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			US 1997-62282	P 19971017
AU	9896928	A1	19990510	AU 1998-96928	19981009
				US 1997-62282	P 19971017
				WO 1998-US21418W	19981009
EP	919234	A2	19990602	EP 1998-308225	19981009
EP	919234	A3	19990825		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			US 1997-62282	P 19971017
US	6066643	A	20000523	US 1998-169369	19981009
				US 1997-62282	P 19971017

AB A method for producing a potentiating effect on a therapeutic action of an agent which is selected from a serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitors, both a serotonin and norepinephrine re-uptake inhibitor, and an atypical antidepressant in a warm blooded mammal, comprises administering to said mammal an effective amt. of moxonidine, or a pharmaceutically acceptable salt thereof. A tablet contained moxonidine 0.300, lactose 95.700, povidone 0.700, crospovidone 3.000, magnesium stearate 0.300, hydroxypropyl Me cellulose 1.300, Et cellulose 1.200, PEG 0.250, talc 0.975, red ferric oxide 0.025, and

titanium dioxide 1.250 mg. Moxonidine at 0.2 mg twice daily when combined with 20 mg fluoxetine daily had synergistic effects in patients suffering major depression.

IT 59729-33-8, Citalopram  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (synergistic pharmaceutical compns. contg. moxonidine)

RN 59729-33-8 CAPLUS  
 CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RE.CNT 1

RE

(1) Armah; US 4952410 A 1990 CAPLUS

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1999:81568 CAPLUS

DN 130:130004

TI Pharmaceutical compositions containing selective serotonin re-uptake inhibitors for the treatment and prevention of cardiac

disorders using

IN Jenner, Paul Norman

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9903469	A1	19990128	WO 1998-GB2073	19980714
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		GB 1997-14841	A 19970714
AU	9883494	A1	19990210	AU 1998-83494	19980714
				GB 1997-14841	A 19970714
				WO 1998-GB2073	W 19980714
EP	996445	A1	20000503	EP 1998-933796	19980714
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI		GB 1997-14841	A 19970714
				WO 1998-GB2073	W 19980714

BR 9811004	A	20000919	BR 1998-11004	19980714
			GB 1997-14841	A 19970714
			WO 1998-GB2073	W 19980714
NO 2000000169	A	20000113	NO 2000-169	20000113
			GB 1997-14841	A 19970714
			WO 1998-GB2073	W 19980714

AB A method for treating and/or preventing cardiac disorders in human or non-human animals comprise administering an effective, non-toxic amt. of a serotonin re-uptake inhibitor (SSRI) or a pharmaceutically acceptable salt thereof. A pharmaceutical tablet contained paroxetine hydrochloride hemihydrate 22.88, dibasic calcium phosphate dihydrate 244.12, hydroxypropyl methylcellulose 15.00, sodium starch glycollate 15.00, and magnesium stearate 3.00 mg. The rate of myocardial infarction for patients who were taking SSRI over 4 yr period was 0.0204 as compared to 0.0226 events/patients year exposure for the general population, showing the patients taking SSRI were statistically less likely to develop a myocardial infarction than those who did not.

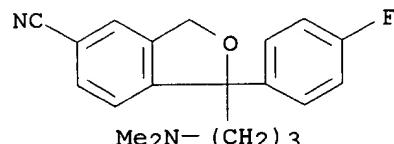
IT 59729-33-8, Citalopram

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. contg. selective serotonin re-uptake inhibitors

for treatment and prevention of cardiac disorders using)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RE.CNT 4

RE

- (1) Carney, R; Clinical Cardiology 1997, V20(3), P196 MEDLINE
- (2) Glassman, A; J Clin Psychiatry 1993, V54(2)
- (3) Pfizer; EP 0768083 A 1997 CAPLUS
- (4) Tikal, K; Psychiatricka Lecebna Kosmonosy Ceskoslovenska Psychiatrie 1993, V89(3), P163 MEDLINE

L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1998:744954 CAPLUS

DN 130:17239

TI **Pharmaceutical composition** and method combining an antidepressant with an NMDA receptor antagonist, for treating neuropathic pain

IN Caruso, Frank S.

PA Algos Pharmaceutical Corp., USA

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9850044	A1	19981112	WO 1998-US9253	19980506
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		US 1997-45900 19970507
AU 9874728	A1	19981127	AU 1998-74728	19980506
			US 1997-45900	19970507
			WO 1998-US9253	19980506
EP 980247	A1	20000223	EP 1998-922115	19980506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, FI			US 1997-45900	19970507
			WO 1998-US9253	19980506

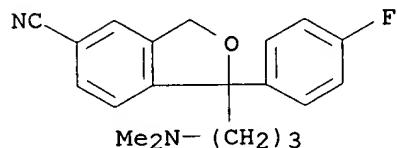
AB The neuropathic pain alleviating effectiveness of an antidepressant is significantly potentiated by administering the antidepressant prior to, with or following the administration of a nontoxic NMDA receptor antagonist. A pharmaceutical capsule contained chlorimipramine hydrochloride 25, and dextromethorphan hydrobromide 30 mg.

IT 59729-33-8, Citalopram

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
**(pharmaceutical compn.** and method combining  
 antidepressant with NMDA receptor antagonist, for treating neuropathic  
 pain)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RE.CNT 8

RE

- (1) Algos Pharm Corp; WO 9627375 A 1996 CAPLUS
- (2) Frome, B; WO 9710815 A 1997 CAPLUS
- (3) Harris, R; WO 9640095 A 1996 CAPLUS
- (4) Lilly Co Eli; EP 0658539 A 1995 CAPLUS
- (5) Smith, R; WO 9609044 A 1996 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2001 ACS  
 AN 1998:402481 CAPLUS

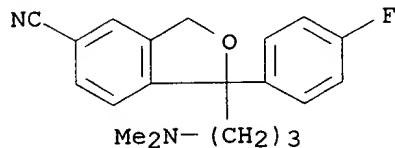
DN 129:19676

TI **Pharmaceutical compositions** for the treatment of  
 depressive disorders

IN Medjad, Nadia; Billardon, Martine

PA UCB, S.A., Belg.  
 SO Pat. Specif. (Petty) (Aust.), 15 pp.  
 CODEN: AUXXDN  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AU 686084	B3	19980129	AU 1997-27539	19970626
				US 1996-672920	19960628
AB	US 5747494	A	19980505	US 1996-672920	19960628
AB	A method for treating a depressive disorder comprises administering to a patient in need thereof a therapeutically effective amt. of a combination (i) hydroxyzine, an individual optical isomer thereof, or a pharmaceutically acceptable salt thereof and (ii) at least one therapeutic substance which is a serotonin uptake inhibitor, an individual optical isomer thereof or a pharmaceutically acceptable salt thereof, the therapeutically effective amt. being such that the depressive disorder is treated while avoiding the nervousness, anxiety, agitation and sleep disorders assocd. with treatments using serotonin uptake inhibitors, and avoiding at the same time the loss of therapeutic effect obsd. when treatment with the classic assocn. of serotonin uptake inhibitors and benzodiazepines is used. A tablet contained fluoxetine.cntdot.HCl 10, hydroxyzine.cntdot.2HCl 25, lactose 200, and Mg stearate 1 mg. Antidepressive effects of the combination were demonstrated with rats.				
IT	59729-33-8, Citalopram RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hydroxyzine and serotonin uptake inhibitor combination for treating depressive disorder with less side effects)				
RN	59729-33-8 CAPLUS				
CN	5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)				



L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2001 ACS  
 AN 1998:204419 CAPLUS  
 DN 128:261968  
 TI **Pharmaceutical composition containing combination of atypical antipsychotic and serotonin reuptake inhibitor for treatment of psychoses**  
 IN Bymaster, Franklin Porter; Perry, Kenneth Wayne; Tollefson, Gary Dennis  
 PA Eli Lilly and Co., USA  
 SO Eur. Pat. Appl., 15 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 830864	A1	19980325	EP 1997-307375	19970922
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			US 1996-26884	P 19960923
	ZA 9707967	A	19990304	ZA 1997-7967	19970904
				US 1996-26884	P 19960923
	WO 9811897	A1	19980326	WO 1997-US15874	19970909
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			US 1996-26884	P 19960923
	AU 9744112	A1	19980414	AU 1997-44112	19970909
	AU 719033	B2	20000504	US 1996-26884	P 19960923
				WO 1997-US15874W	19970909
	BR 9711530	A	19990824	BR 1997-11530	19970909
				US 1996-26884	P 19960923
	CN 1230886	A	19991006	WO 1997-US15874W	19970909
				CN 1997-198113	19970909
	JP 2001503031	T2	20010306	US 1996-26884	P 19960923
				JP 1998-514717	19970909
	US 6147072	A	20001114	US 1996-26884	P 19960923
				WO 1997-US15874W	19970909
	NO 9901381	A	19990322	US 1997-935872	19970923
				US 1996-26884	P 19960923
				NO 1999-1381	19990322
				US 1996-26884	P 19960923
				WO 1997-US15874W	19970909

AB Pharmaceutical compns. contg. combination of atypical antipsychotics and serotonin reuptake inhibitors are useful for the treatment of psychoses. Form II olanzapine (I) polymorph was prep'd. by heating I at 76.degree.

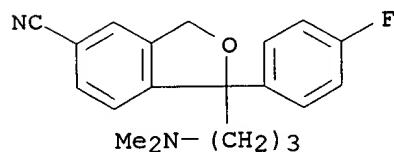
for 30 min in Et acetate and crystn. Hard gelatin capsules contained I 25, fluoxetine hydrochloride 20, starch 150, and magnesium stearate 10 mg.

IT 59729-33-8, Citalopram

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compn. contg. combination of  
atypical antipsychotic and serotonin reuptake inhibitor for treatment  
of psychoses)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

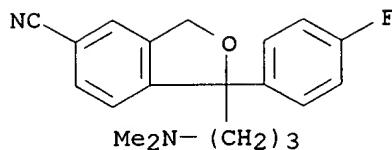


L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2001 ACS  
 AN 1998:21380 CAPLUS  
 DN 128:84406  
 TI **Pharmaceutical composition** comprising mirtazapine and one or more selective serotonin reuptake inhibitors  
 IN Nickolson, Victor Johannes  
 PA Akzo Nobel N.V., Neth.  
 SO Eur. Pat. Appl., 7 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 813873	A1	19971229	EP 1997-201853	19970617
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			EP 1996-201703 A	19960619
	US 5977099	A	19991102	US 1997-876346	19970616
	CA 2208199	AA	19971219	EP 1996-201703 A	19960619
	NO 9702816	A	19971222	CA 1997-2208199	19970618
	BR 9703624	A	19980901	EP 1996-201703 A	19960619
	AU 9726129	A1	19980108	NO 1997-2816	19970618
	AU 727851	B2	20010104	EP 1996-201703 A	19960619
	CN 1173330	A	19980218	BR 1997-3624	19970618
	JP 10067663	A2	19980310	EP 1996-201703 A	19960619
				AU 1997-26129	19970619
				EP 1996-201703 A	19960619
				CN 1997-115549	19970619
				EP 1996-201703 A	19960619
				JP 1997-162576	19970619
				EP 1996-201703 A	19960619

AB The invention relates to a **pharmaceutical compn.** comprising mirtazapine, a selective serotonin reuptake inhibitor (SSRI) and pharmaceutically acceptable auxiliaries. In particular the SSRI is selected from fluoxetine, fluvoxamine, citalopram, cericlamine, femoxetine, sertraline, paroxetine, ifoxetine, cyanodothiepin and litoxetine. The compn. which can be used to treat depressed patients has less side effects than treatment of the patients with mirtazapine or the SSRI alone. When rats were treated with 30 mg/kg fluoxetine s.c., 80 % redn. in food consumption was reported; however, concomitant treatment with 2 mg/kg mirtazapine s.c. resulted in 40 % redn. due to partial antagonism of the appetite-inhibiting effect of fluoxetine by mirtazapine.

IT 59729-33-8, Citalopram  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (mirtazapine and selective serotonin reuptake inhibitor combinations for treatment of depression)  
 RN 59729-33-8 CAPLUS  
 CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2001 ACS  
 AN 1992:400917 CAPLUS  
 DN 117:917  
 TI Use of 1-(3-(dimethylamino)propyl)-1-phenylphthalans derivatives for the treatment of cerebrovascular disorders  
 IN Tanaka, Yoshiaki; Kobayashi, Naomi; Kurimoto, Tadashi; Ikeda, Yugo  
 PA Lundbeck, H., A/S, Den.  
 SO Eur. Pat. Appl., 12 pp.  
 CODEN: EPXXDW

DT Patent

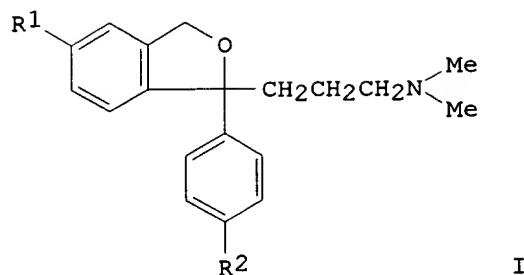
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 474580	A2	19920311	EP 1991-610063	19910816
	EP 474580	A3	19920603		
	EP 474580	B1	19940928		
	R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
				DK 1990-2132	A 19900906
	IL 98968	A1	19960618	IL 1991-98968	19910725
				DK 1990-2132	A 19900906
	ZA 9106187	A	19920429	ZA 1991-6187	19910806
				DK 1990-2132	A 19900906
	CA 2049368	AA	19920307	CA 1991-2049368	19910816
				DK 1990-2132	A 19900906
	KR 9702246	B1	19970226	KR 1991-14255	19910819
				DK 1990-2132	A 19900906
	AU 9182594	A1	19920312	AU 1991-82594	19910820
	AU 644204	B2	19931202		
				DK 1990-2132	A 19900906
	JP 04244024	A2	19920901	JP 1991-224192	19910904
	JP 08005787	B4	19960124		
				DK 1990-2132	A 19900906
	US 5296507	A	19940322	US 1993-1571	19930106
				DK 1990-2132	A 19900906
				US 1991-742907	B119910809

OS MARPAT 117:917

GT



AB The title compds. [I; R1, R2 = halo, CF<sub>3</sub>, cyano, RCO (R = alkyl)] or acid addn. salts thereof are useful in the treatment of dementia, cerebrovascular disorders, and for inhibiting platelet aggregation. Citalopram (II) (40mg/kg) was i.p. injected into gerbils 30 min before carotid occlusion (5 min); 7 days later the animals were killed and surviving neurons were counted. The no. of surviving neurons was 95.8 as compared to 12.8/mm for controls. An injection soln. contained II 10, sorbitol 42.9, acetic acid 0.63, NaOH 22 mg, and water 1mL.

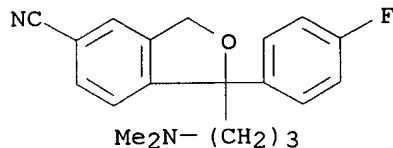
IT 59729-33-8, Citalopram

RL: BIOL (Biological study)

(treatment of cerebrovascular disorders with pharmaceutical compn. contg.)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1992:136283 CAPLUS

DN 116:136283

TI Pharmaceutical preparations for treatment of depression and/or migraine

IN Johnson, Edward Stewart

PA Beecham Group PLC, UK

SO PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9200103	A1	19920109	WO 1991-GB992	19910620
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
			GB 1990-14354	19900628	
			GB 1990-14364	19900628	
			GB 1990-14365	19900628	

AU 9180726	A1	19920123	GB 1990-14367	19900628
			AU 1991-80726	19910620
			GB 1990-14354	19900628
			GB 1990-14364	19900628
			GB 1990-14365	19900628
			GB 1990-14367	19900628
			WO 1991-GB992	19910620
ZA 9104920	A	19920429	ZA 1991-4920	19910626
			GB 1990-14354	19900628

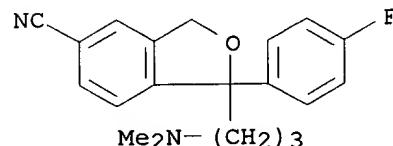
AB A pharmaceutical compn. comprises 2-3 active ingredients selected from a 5-HT3 receptor antagonist, a 5-HT reuptake inhibitor, and a 5-HT1 receptor agonist, as a combined prepn. for simultaneous, sep., or sequential use in therapy.

IT 59729-33-8D, Citalopram, mixt. with 5-HT receptor agonist and 5HT3 receptor antagonists

RL: BIOL (Biological study)  
(pharmaceutical compn. contg., for treatment of depression or migraine)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1990:478150 CAPLUS

DN 113:78150

TI Preparation and isolation of antidepressant drug citalopram enantiomers and their pharmaceutical compositions

IN Boegesoe, Klaus Peter; Perregaard, Jens

PA Lundbeck, H., og Co. A/S, Den.

SO Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DT Patent

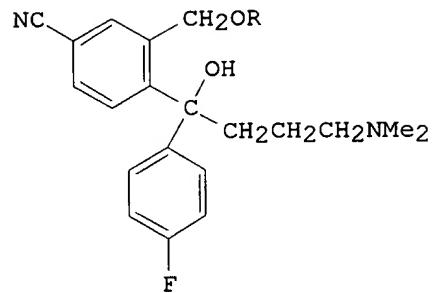
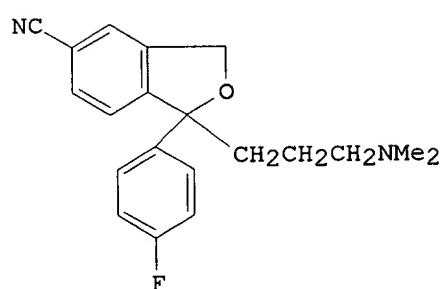
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 347066	A1	19891220	EP 1989-305532	19890601
	EP 347066	B1	19950315		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE			GB 1988-14057	A 19880614
	DK 8902599	A	19891215	DK 1989-2599	19890529
				GB 1988-14057	A 19880614
	IL 90465	A1	19950124	IL 1989-90465	19890530
				GB 1988-14057	A 19880614
	AT 119896	E	19950415	AT 1989-305532	19890601
				GB 1988-14057	A 19880614
	ES 2068891	T3	19950501	ES 1989-305532	19890601
				GB 1988-14057	A 19880614
	FI 8902823	A	19891215	FI 1989-2823	19890608

FI 91527	B	19940331		
FI 91527	C	19940711		
US 4943590	A	19900724	GB 1988-14057 A 19880614	
			US 1989-363589 19890608	
			GB 1988-14057 A 19880614	
NO 8902447	A	19891215	NO 1989-2447 19890613	
NO 172892	B	19930614		
NO 172892	C	19930922		
AU 8936295	A1	19900104	GB 1988-14057 A 19880614	
AU 623144	B2	19920507	AU 1989-36295 19890613	
ZA 8904476	A	19900425	GB 1988-14057 A 19880614	
			ZA 1989-4476 19890613	
			GB 1988-14057 A 19880614	
JP 02036177	A2	19900206	JP 1989-149752 19890614	
JP 3044253	B2	20000522		
DK 9300115	A	19930201	GB 1988-14057 A 19880614	
DK 170280	B1	19950724	DK 1993-115 19930201	
US 34712	E	19940830	GB 1988-14057 A 19880614	
			US 1993-122009 19930914	
			GB 1988-14057 A 19880614	
			US 1989-363589 A519890608	
FI 9401829	A	19940420	FI 1994-1829 19940420	
			GB 1988-14057 A 19880614	
			FI 1989-2823 A 19890608	
CA 1339568	A1	19971202	CA 1997-617069 19970122	
			GB 1988-14057 A 19880614	
			CA 1989-602683 A319890613	
JP 11292867	A2	19991026	JP 1999-46008 19990224	
JP 3038204	B2	20000508		
FI 2000000507	A	20000306	GB 1988-14057 A 19880614	
			JP 1989-149752 A319890614	
			FI 2000-507 20000306	
			GB 1988-14057 A 19880614	

OS MARPAT 113:78150  
GI



AB The title compd. (I) in pure (+)-enantiomer form and its racemic mixt., useful as antidepressants, geriatrics, or in treatment of obesity and alcoholism, are prep'd.  $\text{SOCl}_2$  was refluxed with a soln. of (+)- $\text{CF}_3\text{CH}(\text{OMe})\text{CO}_2\text{H}$  in  $\text{CHCl}_3$  to give the acid chloride, which was dild. with  $\text{CH}_2\text{Cl}_2$  and treated with benzyl alc. deriv. II ( $R = \text{H}$ ) and  $\text{Et}_3\text{N}$  to give ester II [ $R = \text{CF}_3\text{CH}(\text{OMe})\text{CO}$ ] (III) as a diastereomeric mixt., which

MePh was purified by HPLC to give a pure enantiomer. III was dissolved in

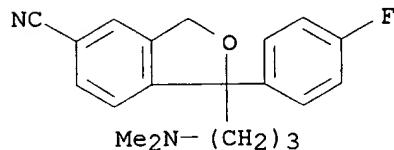
and treated with Me3COK in MePh at 0.degree. to give (+)-I of 99.6% optical purity, which showed ED50 of 2.0 .mu.mol/kg for 5-HTP potentiation

in mice and IC50 of 1.1 nM against 5-HT uptake, vs. 3.3 .mu.mol/kg and 1.8 .mu.M, resp., with (.-.)-I. Similarly prep'd. (-)-I showed much lower activity. Tablet, syrup, and injection formulations were given.

IT 59729-33-8P 128196-03-2P  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as antidepressant)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 128196-03-2 CAPLUS

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2001 ACS

AN 1986:39720 CAPLUS

DN 104:39720

TI Pharmaceutical compositions containing unilamellar liposomes

IN Muntwyler, Rene; Hauser, Helmut

PA Ciba-Geigy A.-G. , Switz.

SO Eur. Pat. Appl., 65 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 152379	A2	19850821	EP 1985-810050	19850211
	EP 152379	A3	19861029		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE			CH 1984-736	19840215
				ES 1985-540372	19850213
	ES 540372	A1	19860601	CH 1984-736	19840215
	CA 1246446	A1	19881213	CA 1985-474204	19850213
	DK 8500685	A	19850816	CH 1984-736	19840215
				DK 1985-685	19850214
	AU 8538753	A1	19850822	CH 1984-736	19840215
	AU 588798	B2	19890928	AU 1985-38753	19850214
				CH 1984-736	19840215
	ZA 8501111	A	19850925	ZA 1985-1111	19850214
				CH 1984-736	19840215
	JP 60190710	A2	19850928	JP 1985-26616	19850215

CH 1984-736 19840215

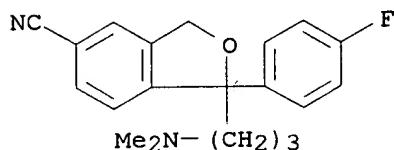
AB Aq. pharmaceutical dispersions made of unilamellar liposomes contg. an amphipathic drug and a phospholipid are given. The amphipathic drugs are quaternary ammonium compds., compds. convertible into quaternary ammonium derivs. by salt formation, .alpha.-amino acids, phosphonic acid esters, etc. Thus, 50 mg soybean lecithin was added to 20.33 mg 1-isopropylamino-3-(2-pyrrol-1-ylphenoxy)propan-2-ol-HCl [99740-06-4] in 30 mL MeOH-CHCl<sub>3</sub> (1:1) in a vial. The vial was rotated, and the film which formed was treated with 1.5 mL H<sub>2</sub>O to give a dispersion of unilamellar liposomes.

IT 59729-33-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(unilamellar liposome pharmaceutical compns. contg.)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)



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L1 1 S E3

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L2 782 S L1  
L3 13 S PHARMACEUTICAL COMPOSITION? AND L2

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 59729-33-8 REGISTRY

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (.+-.)-Citalopram

CN Citalopram

CN Lu 10-171

CN Nitalapram

FS 3D CONCORD

DR 128196-03-2, 103146-27-6

MF C20 H21 F N2 O

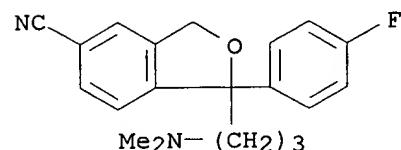
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LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS,  
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DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB,  
IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, PHAR, PROMT, RTECS\*, SYNTHLINE,  
TOXLINE, TOXLIT, USAN, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



777 REFERENCES IN FILE CA (1967 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

780 REFERENCES IN FILE CAPLUS (1967 TO DATE)